Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the amendments and remarks presented herein, is respectfully requested. Claims 22, 25, 30 and 38 have been amended. Claims 22-30, 38-40, 43 and 44 are currently pending.

Examples of support for the amendment of claim 22 and claim 38 are found within the specification at page 12, lines 15-20 and at page 19, lines 22-23. Claims 25 and 30 were amended to correct a spelling error. An example of support for the further amendment of claim 30 to recite a "synergistic amount" is found within the specification at page 13, line 18 to page 14, line 2.

Double Patenting Rejection

Claims 22-29 and 38-39 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent Application No. 10/132,542. Applicants respectfully traverse the provisional rejection of the currently pending claims because the currently pending claims in U.S. Patent Application No. 10/132,542 have not yet been allowed. Accordingly, Applicants respectfully request withdrawal of the provisional rejection of the claims for obviousness-type double patenting.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claim 30 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed. However, in order to expedite prosecution of the above-identified application, Applicants have amended claim 30 to recite a "synergistic amount" of 4-aminopyridine in accordance with the Examiner's suggestion to clarify the claim. Accordingly, reconsideration and withdrawal of the rejection of claim 30 is respectfully requested.

The 35 U.S.C. §102(b) Rejection

The Examiner rejected claims 22, 24-29, and 38-39 under 35 U.S.C. §102(b) alleging that the claims are anticipated by Ducker et al., *J. Neurosurg.*, 30(6):693-697 (1969). This rejection is respectfully traversed.

Ducker discloses the intrathecal administration of a single dose of methylprednisolone to the site of a spinal cord injury in beagles (Ducker at page 694). The methylprednisolone was administered in the form of Depo-medrol® (Ducker, Figure 1).

Depo-medrol® is a trademark for a methylprednisolone acetate formulation that includes benzyl alcohol as a preservative (Exhibit A). Benzyl alcohol is contraindicated for treatment of neural tissue (Exhibit A).

Claim 22, as amended, is directed to a method of treating a mammalian patient having suffered an injury to its spinal cord with a composition comprising at least one C_1-C_{10} polyalkylene glycol in an amount effective to restore nerve impulse conduction through said injured spinal cord. Claim 22 has been amended to recite that the composition does not contain benzyl alcohol.

Claim 38, as amended, is directed to a method of treating a mammalian patient having suffered an injury to its spinal cord with a composition comprising polyethylene glycol in an amount effective to restore nerve impulse conduction through said injured spinal cord. Claim 38 has also been amended to recite that the composition does not contain benzyl alcohol.

Applicants respectfully submit that the specification fully supports a polyalkylene glycol that does not include benzyl alcohol. For example, the specification specifically excludes pharmaceutically carriers that have an adverse effect on a treatment for which the solution is used (page 12, lines 15-20). Therefore, Applicants respectfully submit that no new material has been added by the amendment to claim 22. See, for example, *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187 (CCPA 1977) (holding that "appellants are merely excising the invention of another, to which they are not entitled, and are not creating an 'artificial subgenus' or claiming 'new matter.'" (Exhibit B).

Accordingly, the Examiner is respectfully requested to withdraw the rejection of the claims under 35 U.S.C. § 102 (b) because the cited reference does not teach a composition comprising polyalkylene glycol that does not contain benzyl alcohol.

The 35 U.S.C. §103(a) Rejection

The Examiner rejected claims 22, 24-30, 38-40, and 43-44 under 35 U.S.C. §103(a) as being unpatentable over Balasubramanian (U.S. Patent No. 5,382,584) in view of Potter et al., *Clin. Invest. Med.*, 19(4), Suppl.: S80, #533. This rejection is respectfully traversed.

Balasubramanian teaches that a series of compounds that are 1-piperazinyl-N-phenylacetamide derivatives of 4,5-diphenyl-oxazoles, thiazoles, and imidazoles were found to provide effective antiischemic protection for central nervous system and cardiac tissue, particularly neurons (Abstract). The compounds were described as novel adenosine reuptake inhibitors (column 1, lines 19-22). The compounds are generally given as pharmaceutical compositions containing at least one compound and a pharmaceutically acceptable carrier (column 5, lines 11-16). The pharmaceutically acceptable carrier comprises one or more solid, semi-solid, or liquid diluent, filler and formulation adjuvant which is non-toxic, inert and pharmaceutically acceptable (column 5, lines 20-23, emphasis added).

Potter discloses that 4-aminopyridine is a K+ channel blocking agent that enhances nerve conduction through areas of demyelination in patients with spinal cord injuries.

Claim 22 recites, *inter alia*, a method of treating a mammalian patient having suffered an injury to its spinal cord with a composition comprising at least one C_1-C_{10} polyalkylene glycol in an amount effective to restore nerve impulse conduction through said injured spinal cord.

Claim 38 recites, *inter alia*, a method of treating a mammalian patient having suffered an injury to its spinal cord with a composition comprising polyethylene glycol in an amount effective to restore nerve impulse conduction through said injured spinal cord.

Applicants respectfully submit that the Examiner has not met the burden of establishing a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three criteria must be met. First, the prior art reference (or references) must teach or suggest all of the claim

limitations. Second, there must be some suggestion or motivation, either in the cited reference (or references), or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Third, there must be a reasonable expectation of success. M.P.E.P. § 2142 (citing *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991)).

Applicants submit that neither Balasubramanian nor Potter teach or suggest all of the claim limitations because, for example, neither reference teaches the use of a composition comprising at least one C_1-C_{10} polyalkylene glycol in an amount effective to restore nerve impulse conduction through an injured spinal cord in a mammal having a spinal cord injury. Balasubramanian generally teaches that a vehicle consisting of a polyhydridic aliphatic alcohol such as glycerine, propylene glycol, and the polyethylene glycols or mixtures thereof is acceptable for use in preparing compositions for parenteral administration of an antiischemic compound, however, such vehicles are described as being inert (column 5, lines 16-23 and column 6, lines 12-27). The inert character of the pharmaceutical carriers used by Balasubramanian is further indicated by the results they obtained using a canine model of cardiac infarct size reduction in which the cardiac infarct size in dogs treated with formula I compounds was reduced when compared to animals treated with the vehicle alone (column 4, lines 40-46). The vehicle alone was not reported to have any effect when used within the model assay. Accordingly, Applicants submit that the compositions taught in Balasubramanian exclude polyalkylene glycols in the amounts effective for the treatment of neural tissue (e.g., claim 1) because such polyalkylene glycols are not inert when applied to the neural tissue. Potter is silent regarding the use of any polyalkylene glycol and is cited only for the use of the K+ channel blocker, 4-aminopyridine. Accordingly, not only do the cited references, alone or in combination, fail to teach or suggest all of the claim limitations, Balasubramanian actually teaches away from the claimed invention.

Applicants further submit that there is no suggestion or motivation to combine the disclosure of Balasubramanian with that of Potter. Balasubramanian is directed to antiischemic compounds that are adenosine reuptake inhibitors. Potter, on the other hand, describes 4-aminopyridine as a K+ channel blocking agent. Neither reference discloses that 4-aminopyridine

is an adenosine reuptake inhibitor or that it has any antiischemic activity. Furthermore, neither reference discloses any suggestion to combine an antiischemic agent with a K+ channel blocking agent.

Applicants also contend that there is no expectation of success in combining the disclosure of Balasubramanian with that of Potter. Balasubramanian teaches that agents that increase adenosine levels in ischemic tissue should result in enhanced neuroprotection (column 4, line 7-9). Potter teaches that 4-aminopyridine is a K+ channel blocking agent, but does not teach that 4-aminopyridine increases adenosine levels in ischemic tissue. Accordingly, neither reference, alone or in combination, provides an expectation of success that 4-aminopyridine would have any antiischemic activity, or that it would provide any antiischemic protection to any tissue.

Applicants submit that the Examiner has not met the burden of establishing a *prima facie* case for the aforementioned reasons. Accordingly, withdrawal of the rejections of the claims under 35 U.S.C. § 103 is respectfully requested.

The Examiner rejected claims 30, 40 and 43-44 under 35 U.S.C. §103(a) alleging that the claims are unpatentable over Ducker et al., *J. Neurosurg.*, 30(6):693-697 (1969) in view of Potter et al., *Clin. Invest. Med.*, 19(4), Suppl S80 #533. This rejection is respectfully traversed with respect to the currently pending claims.

As noted above, claim 22 has been amended to recite to a method of treating a mammalian patient having suffered an injury to its spinal cord with a composition comprising at least one C_1-C_{10} polyalkylene glycol in an amount effective to restore nerve impulse conduction through said injured spinal cord, wherein the composition does not contain benzyl alcohol. Likewise, claim 38 has been amended to recite a method of treating a mammalian patient having suffered an injury to its spinal cord with a composition comprising polyethylene glycol in an amount effective to restore nerve impulse conduction through said injured spinal cord, wherein the composition does not contain benzyl alcohol.

As described in detail in connection with the rejection under 35 U.S.C. §102(b) above, neither Ducker nor Potter teach or suggest all of the claim limitations because neither reference

discloses use of a composition that does not contain benzyl alcohol to restore nerve impulse conduction through an injured spinal cord in a mammal.

In addition, there is no expectation of success in combining the disclosure of Ducker with that of Potter. Ducker discloses that a single dose of methylprednisolone (Depo-medrol®) 8 mg/kg was delivered intrathecally directly at the site of trauma (page 694). Potter disclosed that patients having temperature-dependent central conduction deficits who received intervenous 4-aminopyridine (24 mg total dose) demonstrated improved volitional EMG (electromyography) interference patterns, but the changes were reversed after drug washout. Therefore, the disclosure of Potter teaches that a single dose of 4-aminopyridine, as would be used in accordance with the disclosure of Ducker, would not be useful for treatment of a spinal cord injury.

Applicants submit that the Examiner has not met the burden of establishing a *prima facie* case for the aforementioned reasons. Accordingly, withdrawal of the rejections of the claims under 35 U.S.C. § 103 is respectfully requested.

Information Disclosure Statement

Applicants submit herewith a Supplemental Information Disclosure Statement, including 1449 form(s) and copies of the documents cited thereon. Consideration of the documents cited on the accompanying 1449 form(s), and return of an initialed copy of the 1449 form(s) indicating consideration of said documents with the next Official Communication, is respectfully requested.

Summary

It is respectfully submitted that pending claims 22-30, 38-40, 43, and 44 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.10:
"Express Mail" mailing label number: EV073 737 220US Date of Deposit: 27 February 2004
The undersigned hereby certifies that the Transmittal Letter and the paper(s) and/or fee(s), as described hereinabove, are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents,P.O. Box 1450, Alexandria, VA 22313-1450.

By: _____
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The Examiner is invited to contact Applicants' Representatives at the below-listed telephone number, if they can be of any assistance during prosecution of the present application.

CERTIFICATE UNDER 37 C.F.R. 1.10:

The undersigned hereby certifies that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated below and is addressed to the Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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